

UDC 666.3:546'41

## POROUS MATERIALS MADE FROM CALCIUM PHOSPHATES (REVIEW)

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Translated from *Steklo i Keramika*, No. 10, pp. 17 – 19, October, 2008.

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The methods of fabricating porous materials are reviewed. The optimum methods of fabricating porous materials from calcium phosphates, including materials for use as bone implants, are demonstrated.

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Porous materials are used for fabricating bone implants and particularly for treating nonextensive bone defects not subject to mechanical loads. The phase composition of these materials must be represented by biocompatible inorganic components with predominance of the biodegradable (resorbable) phase [1]. The pores in these materials must be permeable, and their size must be large enough, a minimum of 100  $\mu\text{m}$ , to ensure penetration of physiological medium inside the material. The strength of the material must be sufficient for the physician to perform the necessary manipulations both in the stage of preparing the implant and during the surgery. When replacing a bone defect, such porous material creates conditions initially for formation of a man-made inorganic material – organic component composite, and then a regenerated hydroxyapatite carbonate – organic component composite.

There are methods for fabrication of porous materials using the polymer matrix duplication method [2, 3] based on calcium phosphate powders (US Patent No. 7037869 B2) [4]; mixtures of powdered calcium phosphate and glasses from the  $\text{MgO} - \text{CaO} - \text{SiO}_2 - \text{P}_2\text{O}_5 - \text{CaF}_2$  or  $\text{SiO}_2 - \text{Na}_2\text{O} - \text{CaO} - \text{P}_2\text{O}_5$  system [5] based on powdered glass from the  $\text{MgO} - \text{CaO} - \text{SiO}_2 - \text{P}_2\text{O}_5$  system, whose phase composition after burning was represented by tricalcium phosphate and diopside [6]; mixtures of powdered hydroxyapatite and wollastonite [7]; mixture of hydroxyapatite and glass powder from the  $\text{CaO} - \text{P}_2\text{O}_5$  system [8].

Polyurethane foam is primarily used as the porous polymer matrix in these methods. The method allows duplicating the pore structure of the polymer matrix. Its undoubted advantage is that production of polyurethane foam with different pore size and pore size distribution, impregnation of slips made of different materials, and drying and heat treat-

ment that ensure production of a highly permeable ceramic, including those made of calcium phosphates, have been mastered in industry. At the same time, toxic gases are liberated when the polyurethane matrix is burned out and they must be eliminated and detoxified.

This technology was used at D. I. Mendeleev Russian Chemical Engineering University to create a highly porous (up to 90% porosity) ceramic with a honeycomb structure from hydroxyapatite for use as bone implants. Several operations were performed to treat bone defects. Observations of the behavior of the implants showed that the resorption rate was approximately two times higher than with other biomaterials used for plastic bone surgery.

The method of fabricating the porous materials for bone implants based on natural coral involves treating it with soluble compounds containing phosphate ions, such as phosphoric acid or ammonium hydrophosphate. During heat treatment, the coral (calcium carbonate,  $\text{CaCO}_3$ ) reacts with  $\text{H}_3\text{PO}_4$  or  $(\text{NH}_3)_2\text{HPO}_4$ , forming one- (hydroxyapatite), two-phase (hydroxyapatite – tricalcium phosphate or tricalcium phosphate – pyrophosphate), or three-phase (hydroxyapatite/tricalcium phosphate/pyrophosphate) material (US Patent No. 4861733). In topochemical conditions of conducting the reaction, the pore structure of the coral can be inherited.

There are methods of fabricating porous materials, including calcium phosphate materials, using a matrix of closely packed spheres of an inorganic material [2], for example, monodisperse polystyrene latex spheres [9], polymethyl methacrylate [10, 11], paraffin, etc., which burns out or is eliminated on heating. These are versions of the burn additive method, which is well-known in ceramics technology for fabrication of porous materials. The material can be obtained by firing stock molded from a mixture of calcium phosphate powder and polymethyl methacrylate spheres (US Patent No. 4963145) [12] or from a mixture of glass powder from the  $\text{SiO}_2 - \text{CaO} - \text{K}_2\text{O}$  system and polyethylene spheres [13].

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Use of paraffin is promising, since it can be recycled after melting out of the stock. After removal of paraffin, the pore walls can be additionally compacted in a hydrostat after first filling the pores with a liquid. A drawback of the method is that spheres of the required size must be prepared in advance.

There are methods of manufacturing porous calcium phosphate materials using camphene or water as the blowing agent [14, 15]. Porosity appears when the stock is frozen, so that regions consisting primarily of camphene or ice are formed, and after they are removed, pores are formed. The advantage of camphene is its high volatility, which allows removing it by sublimation and collecting and recycling it. Use of water requires using water-soluble polymers that polymerize in freezing, for example, polyvinyl alcohol, and no problems with liberation of harmful gases arise. The drawback of these methods is that the pore size is difficult to control.

Molding from foamed slip is used for manufacturing porous calcium phosphate materials (US Patents Nos. 4963145 and 6511510) [3, 16, 17]. Water-soluble polymers which form a stable and relatively rapidly hardening foam are added to the slip. A drawback of these methods is the necessity of selecting the polymers, hardening methods, and rigorously controlling the rheological properties of the slip.

There is a method of fabricating porous materials by sintering glass powders containing blowing agents, usually carbonates, in the amount of 1 – 5% [18, 19]. Technologies in which gas formation in systems containing melted glass occurs are widely used, primarily for production of heat- and sound-insulating construction materials [20]. “The process parameters were developed for glass powders close in chemical composition to window glass. The method allows obtaining highly porous permeable materials, which also makes it attractive for manufacturing bone implants. At the same time, the rheological properties of the melt must be rigorously controlled and the process parameters (batch composition, heat treatment regimes) of powdered systems made of materials for bone implants. When this method is used, it is also somewhat difficult to control the number and size of the pores, as well as their distribution by size.

There is a method for fabricating a porous material with the  $\text{SiO}_2 - \text{CaO} - \text{Na}_2\text{O} - \text{P}_2\text{O}_5$  system that includes melting the batch, fritting the melt obtained, grinding the frit to a powder, molding the glass powder with addition of a blowing agent, hot molding or two-stage firing of the mixture. Calcium carbonate, sodium carbonate and hydrocarbonate, and ammonium dihydrophosphate (US Patent No. 5676720) were used as the blowing agent. A drawback of this method is the necessity of first melting and grinding the glass from which the porous material is formed during firing or in the hot molding stage.

Material made from neutral aluminoborosilicate glass filled with hydroxyapatite powder can be fabricated by the foaming method (RF Patent No. 2053737). This method allows using glass containing sodium and phosphorus oxides that increase the solubility of the glass matrix. A similar ma-

terial (RF Patent No. 2074672) contained other, more soluble calcium phosphates together with hydroxyapatite as filler.

Fabrication of a bioactive microporous material containing calcium phosphate, a glass matrix, and a blowing agent is described in [19]. A drawback of this method is the necessity of preliminary melting and grinding of the glass from which the glass matrix is formed during firing.

A porous material based on calcium phosphate can be made from a batch containing an alkali metal acetate and an alkali metal hydroxide, in addition to calcium phosphate powder (RF Patent Application No. 2008113835). This method eliminates the stage of melting and subsequent grinding of the glass forming the glass matrix of the porous material. On heating, the potassium  $\text{KCH}_3\text{COO}$  or sodium  $\text{NaCH}_3\text{COO}$  alkali metal acetate, and then the potassium  $\text{KOH}$  or sodium  $\text{NaOH}$  hydroxide melt, perhaps with formation of an eutectic mixture, which ensures uniform distribution of the added component in the powdered stock. The melt containing  $\text{KOH}$  or  $\text{NaOH}$ , which will be aggressive with respect to calcium phosphate, dissolve it from the surface. The melt becomes rich in phosphorus and calcium oxides. At temperatures above  $400^\circ\text{C}$ , the potassium or sodium acetate decomposes with formation of potassium  $\text{K}_2\text{CO}_3$  or sodium  $\text{Na}_2\text{CO}_3$  and  $\text{K}_2\text{Ca}(\text{CO}_3)_2$  or  $\text{Na}_2\text{Ca}(\text{CO}_3)_2$  double carbonates.

Above  $800^\circ\text{C}$ , the stock contains carbonates and a melt of complex, hypothetically eutectic, composition in the  $\text{CaO} - \text{P}_2\text{O}_5 - \text{K}_2\text{O} - \text{CO}_2$  or  $\text{CaO} - \text{P}_2\text{O}_5 - \text{Na}_2\text{O} - \text{CO}_2$  system, together with calcium phosphate particles. On further heating, the potassium, sodium, and calcium carbonates present in the burned stock decompose. The presence of a melt in the material and liberation of gases caused by decomposition of the carbonates results in formation of porous calcium phosphate material. It should be noted that when the foaming method is used, the material used could form glassy composites with high viscosity, which imposes limitations on the compositions used.

As a consequence, methods developed for highly porous materials in glass and ceramics technology are used for fabrication of highly porous bone implants. A specific feature of bond implants is the more severe requirements for their purity, chemical and phase compositions, and reproducibility of working properties. For implants, it is very important to be able to control the number and size of the pores and the pore size distribution. In this respect, the polymer matrix duplication method and method for removal of a matrix created from contacting spheres that form a system of open pores present the greatest possibilities.

*The study was conducted within the FTP “Research and Development in Priority Directions of Development of the Russian Scientific and Manufacturing Complex for 2007 – 2012” and with the support of RFFI Grants 07-08-00576 and 05-03-32768.*

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